United States Court of Appeals

for the

District of Columbia Circuit

AMICUS CURIAE BRIEF

IN THE
United States Court of Appeals
FOR THE DISTRICT OF COLUMBIA CIRCUIT

Nos. 84-1252, 84-1392 and 85-1014

PUBLIC CITIZEN HEALTH RESEARCH GROUP, *et al.*,
Petitioners,
v.
ROBERT A. ROWLAND, Assistant Secretary of Labor
Occupational Safety and Health Administration, *et al.*,
Respondents,
and
ASSOCIATION OF ETHYLENE OXIDE USERS,
Petitioners,
v.
ROBERT A. ROWLAND, Assistant Secretary of Labor
Occupational Safety and Health Administration, *et al.*,
Respondents,

On Petitions for Review to the
Occupational Safety and Health Administration

MOTION OF ETHYLENE OXIDE INDUSTRY COUNCIL FOR LEAVE TO FILE BRIEF AMICUS CURIAE

The Ethylene Oxide Industry Council ("EOIC") of the Chemical Manufacturers Association respectfully requests permission to file the attached brief *amicus curiae* in support of respondent Occupational Safety & Health Administration ("OSHA").

STATEMENT OF INTEREST

The EOIC, which operates as a special program of the Chemical Manufacturers Association, represents both producers and users of ethylene oxide ("EO"). The producer members of the EOIC account for over 90 percent of domestic production of EO. User members include companies that convert EO to other products, as well as companies that use EO in the manufacture of food, pharmaceutical, cosmetic, medical and health products. All of these members are subject to the new OSHA standard on EO. Industry trade associations, such as the Health Industry Manufacturers Association, the Pharmaceutical Manufacturers Association, the American Spice Trade Association, and INDA Association of Non-woven Fabrics Industry, also belong to the EOIC.

The primary objectives of the EOIC are to develop and to communicate information regarding responsible industry programs to control exposure to EO, to generate scientific and other information regarding EO, and to work with government bodies considering regulatory controls pertaining to EO, to ensure that any such regulations are reasonable, scientifically sound, health protective and economically effective. In furtherance of these objectives, EOIC has, among other things, contracted with Dr. Leon Golberg, a renowned toxicologist, to prepare a comprehensive hazard assessment for EO. The EOIC participated extensively in all aspects of the OSHA rulemaking proceedings, including the submission of comprehensive written comments and other scientific materials. The EOIC also presented a number of scientific witnesses, including Dr. Golberg, at the OSHA hearing.

REASONS FOR BRIEF *AMICUS CURIAE*

The EOIC is submitting the attached brief to address only one issue—the OSHA decision not to issue a short-term exposure limit for EO. The purpose of the brief is to bring to this Court's attention portions of the record that have been omitted or mischaracterized in the brief of petitioner Public Citizen Health Research Group. The EOIC believes that the record before OSHA, when properly viewed as a whole, demonstrates that there is no scientific basis for a short-term exposure limit. The attached brief *amicus curiae* is submitted to present the EOIC view of the record regarding short-term exposures, in order to assist this Court in reviewing this aspect of the revised standard.

POSITION OF THE PARTIES

Counsel for the EOIC has contacted counsel for each of the parties to this matter, and is authorized to represent to this Court that the parties do not object to the filing of the attached brief *amicus curiae*, provided that it is filed within the time permitted for OSHA to file its brief.

Respectfully submitted,

ROBERT C. BARNARD
ERIC C. JEFFREY
CLEARY, GOTTLIEB, STEEN
& HAMILTON
1752 N Street, N.W.
Washington, D.C. 20036
(202) 728-2700
Counsel for Amicus Curiae
Ethylene Oxide
Industry Council

Of Counsel:
DAVID ZOLL
General Counsel
CHEMICAL MANUFACTURERS
ASSOCIATION
2501 M Street, N.W.
Washington, D.C. 20037
(202) 887-1100

May 8, 1985

BRIEF *AMICUS CURIAE*

TABLE OF CONTENTS

Page

INTRODUCTION 1

ISSUE PRESENTED 5

STATEMENT OF THE CASE 5

ARGUMENT

OSHA's DECISION IS SUPPORTED BY THE RECORD 7

I. DATA ON DOSE-RATE EFFECTS ARE NECESSARY TO SUPPORT A SHORT-TERM EXPOSURE LIMIT 8

A. Data On Dose Rate Are Essential To Determine If A Short-Term Exposure Limit Will Reduce A Significant Risk 8

B. Data On Dose-Rate Effects Are Of Particular Importance For EO, Because The PEL Will Itself Result In Low Short-Term Exposure Levels 9

C. The Record Amply Demonstrates The Need For Dose-Rate Data 12

II. THERE ARE NO SCIENTIFIC DATA TO SUPPORT A SHORT-TERM EXPOSURE LIMIT 16

A. The Available Studies Do Not Support A Short-Term Exposure Limit 16

B. PCHRG's Speculations On Dose-Rate Effect Do Not Provide Substantial Evidence 22

III. OSHA HAS MADE THE APPROPRIATE RESPONSE OF REQUESTING FURTHER STUDY 23

CONCLUSION 24

TABLE OF AUTHORITIES

Cases: Page

American Textile Manufacturers Institute v. *Donovan*, 452 U.S. 490 (1981) 7
**Industrial Union Department, AFL-CIO* v. *American Petroleum Institute*, 448 U.S. 607 (1980) 7, 9, 16
Public Citizen Health Research Group v. *Auchter*, 702 F.2d 1150, 226 U.S. App. D.C. 413 (D.C. Cir. 1983) 3

Statutes, Regulations and Federal Register Notices:

29 U.S.C. § 655(f) 7
*49 Fed. Reg. 25734 (June 22, 1984) 6, 11, 16, 18
*50 Fed. Reg. (January 2, 1985) 7

Other Authorities:

American Conference of Governmental Industrial Hygienists, Threshold Limit Values for Chemical Substances in the Work Environment Adopted by ACGIH for 1984-85 (1984) 2

---

* Cases or authority chiefly relied upon are marked by asterisks.

IN THE

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Nos. 84-1252, 84-1392 and 85-1014

PUBLIC CITIZEN HEALTH RESEARCH GROUP, *et al.*,
Petitioners,
v.
ROBERT A. ROWLAND, Assistant Secretary of Labor
Occupational Safety and Health Administration, *et al.*,
Respondents,
and
ASSOCIATION OF ETHYLENE OXIDE USERS,
Petitioners,
v.
ROBERT A. ROWLAND, Assistant Secretary of Labor
Occupational Safety and Health Administration, *et al.*,
Respondents,

On Petitions for Review to the
Occupational Safety and Health Administration

BRIEF AMICUS CURIAE OF THE ETHYLENE OXIDE INDUSTRY COUNCIL

INTRODUCTION

The Ethylene Oxide Industry Council ("EOIC") of the Chemical Manufacturers Association respectfully submits this brief *amicus curiae* in support of the decision of the Occupational Safety and Health Administration ("OSHA") not to issue a short-term exposure limit [1] for ethylene oxide ("EO"). The OSHA decision not to promulgate a short-term exposure limit is amply supported by the record.

---

[1] The term "STEL" has been used by many participants in the rulemaking to represent a number of differing concepts. The

The EOIC is a special program of the Chemical Manufacturers Association representing both producers and users of EO. It was organized in July 1981, following completion of an industry-funded rat inhalation study on EO conducted at the Bushy Run Research Center (Exhibit 56).[2] The primary objectives of the EOIC are to develop and to communicate information regarding responsible industry programs to control exposure to EO, to generate scientific and other information regarding EO, and to work with government bodies considering reg-

---

American Conference of Governmental Industrial Hygienists ("ACGIH") states that a STEL is:

> the concentration to which workers can be exposed continuously for a short period of time without suffering from 1) irritation, 2) chronic or irreversible tissue damage, or 3) narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency, and provided that the daily TLV-TWA is not exceeded. It is not a separate independent exposure limit, rather it supplements the time-weighted average (TWA) limit where there are recognized acute effects from a substance whose toxic effects are primarily of a chronic nature. STELs are recommended only where toxic effects have been reported from high short-term exposures in either humans or animals.

ACGIH, Threshold Limit Values for Chemical Substances in the Work Environment adopted by ACGIH for 1984-85, at 3. Another type of limit which has sometimes been mistakenly referred to as a STEL is an internal operating limit that may be used by some companies for short-term exposures. This type of short-term limit, discussed below in footnote 10, is not based on health effects, but is instead designed as an operating guideline to be utilized as a useful engineering method to help control cumulative exposures to the desired daily limit. In this brief, the EOIC will use the term "short-term exposure limit" to refer to a regulatory limit based on health effects, and the term "internal operating guidelines" to refer to the engineering based internal controls.

[2] Exhibits to the OSHA record will be cited herein as Exhibit ——. References to testimony at the hearing on EO will be in the form Tr. ——.

ulatory controls pertaining to EO, in order to ensure that any such regulations are reasonable, scientifically sound, health protective and economically effective.[3]

The members of the EOIC account for over 90 percent of domestic production of EO and cover a broad spectrum of EO users, including companies that convert EO to other products, as well as companies that use EO in the manufacture of food, pharmaceutical, cosmetic, medical and health products. Industry trade associations, such as the Health Industry Manufacturers Association, the Pharmaceutical Manufacturers Association, the American Spice Trade Association and INDA Association of Nonwoven Fabrics Industry, also belong to the EOIC.

The EOIC is principally involved in the development and communication of scientific and technological information regarding EO. In particular, the EOIC contracted with Dr. Leon Golberg, an eminent toxicologist now at Duke University, to supervise the preparation of a comprehensive hazard assessment for EO and to provide a scientific evaluation of the potential hazard at various exposure levels. A copy of his Hazard Assessment (Exhibit 47) and a post-hearing supplement (Exhibit 141 item A) were provided to OSHA, along with peer review comments by two prominent toxicologists. (Exhibits 48, 49). The Hazard Assessment, having undergone further prepublication peer review, is in the process of being published by CRC Reviews.

The EOIC also participated extensively in the OSHA rulemaking proceedings that resulted in the issuance of the standard establishing a new permissible exposure limit ("PEL") of 1 ppm, measured as an eight-hour time-weighted average ("TWA"). The EOIC submitted comprehensive written comments and other scientific information to OSHA at all stages of the rulemaking. In addition, the EOIC presented detailed scientific testimony at the OSHA hearings on EO, including presentations by Dr. Golberg and other scientists.

---

[3] As this Court noted in an earlier opinion relating to the OSHA rulemaking regarding EO, industry has taken the initiative in recognizing and responding to the potential risks posed by occupational exposure to EO. *Public Citizen Health Research Group* v. *Auchter*, 702 F.2d 1150, 1152 n.3, 1155 (D.C. Cir. 1983). A summary of the testing and protective measures taken by industry can be found in the EOIC Comments on the Advanced Notice of Proposed Rulemaking issued by OSHA on January 26, 1982. (Exhibit 4-33).

In this brief *amicus curiae*, the EOIC will address only a single issue relating to the new standard for EO—OSHA's decision not to promulgate a short-term exposure limit. As the EOIC has consistently stated, it does not object to the new PEL of 1 ppm (TWA). The EOIC believes that the 1 ppm PEL is highly conservative,[4] and that the standard is health protective and generally achievable with difficulty, through the use of respirators in certain potential exposure situations.

The position of the EOIC regarding the short-term exposure limit is that the OSHA decision is fully supported by the record as a whole. The purpose of this brief is to highlight important aspects of the record that were either omitted or improperly characterized by petitioner Public Citizen Health Research Group ("PCHRG"). When the entire record is reviewed, it is clear that OSHA acted correctly in determining that the available evidence is not sufficient to support a short-term exposure limit, because there are no data supporting a finding of significant risk from short-term exposures apart from their contribution to cumulative exposure (which is already controlled by the new standard).[5]

---

[4] The EOIC position on the conservative nature of the standard is based on the Hazard Assessment prepared by Dr. Golberg. Dr. Golberg characterized the hazard from EO as falling into three zones: above 10 ppm (TWA), from 1 ppm to 10 ppm, and at or below 1 ppm. The zone of exposure levels at or below 1 ppm (TWA) was judged to pose no significant risk. (Exhibit 47 at 162). Petitioner Public Citizen Health Research Group mischaracterizes the EOIC position by claiming that the EOIC found a higher residual risk than did OSHA at 1 ppm (TWA). (PCHRG brief at 17 n.7). The numbers cited by PCHRG are *not* estimates of risk, as PCHRG is well aware. They are instead the results of mathematical modeling in the extrapolation from high dose to low doses and from animals to man, which were evaluated by Dr. Golberg along with other data in characterizing the potential human hazard from exposure to EO.

ISSUE PRESENTED

The sole issue to be addressed in this *amicus curiae* brief is whether OSHA may be required to issue a short-term exposure limit, in addition to the new PEL, where there is no evidence that short-term exposures present any significant risk apart from their contribution to cumulative exposure. In particular, the brief will focus on the evidence in the record demonstrating (1) that a short-term exposure limit must be supported by data showing that there is a significant risk attributable to the *rate* at which exposure occurs (so-called dose-rate effects), as opposed to the total or cumulative exposure (generally known as dose-response), and (2) that there are no such data for EO.[6]

STATEMENT OF THE CASE

The relevant factual background regarding the issue of short-term exposures can be succinctly stated as follows.

1. During the rulemaking proceedings leading up to the issuance of the revised standard for EO, one of the many issues addressed by OSHA and by participants was

---

[5] The EOIC does not believe it necessary to address the role of the Office of Management and Budget ("OMB") with respect to the OSHA decision on short-term exposures. The record before the Administrator when he made his decision on a short-term exposure limit demonstrates so compellingly the lack of substantial evidence for such a limit that a contrary decision would have been without support in the record.

[6] This action was before this Court previously on a motion by the Association of Ethylene Oxide Users for a stay, which was denied by this Court on January 23, 1985. A related case has also been before this Court. *Public Citizen Health Research Group* v. *Auchter*, 702 F.2d 1150 (D.C. Cir. 1983).

the propriety of a short-term exposure limit for EO. PCHRG and various unions took the position that a short-term exposure limit was appropriate. The EOIC and other industry parties argued that a short-term exposure limit for EO was not supported by the scientific evidence.

2. On or about June 14, 1984, OSHA transmitted to the Office of Management and Budget ("OMB") a proposed, unsigned draft of a revised standard for EO. (Exhibit 167B). The draft sent to OMB contained, among other things, provisions for a short-term exposure limit of 10 ppm, measured over a 15-minute period. OMB sent a letter to OSHA providing its comments on a number of issues relating to the standard, including the proposed short-term exposure level. (Exhibit 162). In its comments on the short-term exposure limit, OMB pointed out that OSHA had failed to adequately address several issues that were necessary to support such a limit.

3. Upon reviewing the OMB comments, OSHA decided that the evidence regarding short-term exposures was subject to sufficient scientific dispute that it would be approriate to obtain further scientific peer review. Accordingly, when OSHA issued the final standard on June 22, 1984, it specifically reserved decision on the short-term exposure limit and set up a two-tier process for obtaining further information. 49 *Fed. Reg.* 25734, 25775.

4. As part of this two-tier process, OSHA sent relevant material to members of the National Advisory Committee on Occupational Safety and Health and a variety of other scientific peer reviewers. (Exhibits 168, 169). A majority of the peer reviewers, including a large majority of the independent (non-party, non-governmental) peer reviewers, opposed the imposition of a short-term exposure limit. A primary basis for their opposition to the short-term exposure limit was the absence of data demonstrating a dose rate effect for EO.

5. On January 2, 1985, OSHA issued its decision regarding the proposed short-term exposure limit. 50 *Fed. Reg.* 64. OSHA determined, based on all of the evidence in the record, that a short-term limit was "not reasonably necessary and appropriate for inclusion in the final EtO standard." *Id.* The bases for OSHA's decision were: (1) that the data do not indicate that short-term exposures to EO pose any risks apart from their contribution to cumulative exposures; (2) that the potential effects of EO appear to depend mainly on cumulative dose, therefore indicating the adequacy of the 1 ppm PEL to minimize significant risk; and (3) that the engineering controls and industrial hygiene practices that will be implemented to meet the 1 ppm PEL and 0.5 ppm action level will result in appropriate control of short-term exposures.

ARGUMENT

OSHA'S DECISION IS SUPPORTED BY THE RECORD

The Supreme Court has held that OSHA may not lower an exposure limit regarding a particular substance unless it finds, based on substantial evidence in the record as a whole (29 U.S.C. § 655(f)), that: (1) there is a significant risk of health impairment at the existing exposure level, and (2) reduction of the exposure level is necessary to achieve a significant reduction in that risk. *Industrial Union Department, AFL-CIO v. American Petroleum Institute*, 448 U.S. 607, 639-40, 642 (plurality), 664-65 (Powell, J., concurring) (1980). *See American Textile Manufacturers Institute v. Donovan*, 452 U.S. 490 (1981). OSHA has found that there is no substantial evidence indicating that short-term exposures present a significant risk (different from the risk of cumulative exposure controlled by the new PEL) or that a short-term exposure limit would make any significant contribution to the reduction of a significant risk. This finding is fully supported by the record. OSHA thus properly declined to impose a short-term exposure limit in addition to the new 1 ppm PEL. Indeed, in the absence of substantial evidence that such a limit would significantly reduce a significant risk, OSHA was not authorized to issue a short-term exposure limit.

I. DATA ON DOSE-RATE EFFECTS ARE NECESSARY TO SUPPORT A SHORT-TERM EXPOSURE LIMIT

A. Data On Dose Rate Are Essential To Determine If A Short-Term Exposure Limit Will Reduce A Significant Risk

There are two basic types of exposure limits that can be used to reduce the potential risk associated with exposure to a particular substance. A PEL or TWA limit reduces cumulative exposure to the substance (generally measured over an eight-hour day). A short-term exposure limit operates as an additional restraint on exposures within the PEL. Such a limit requires that exposures for each short period of time during the work day (often 15 minutes) be kept below a specified level. Thus, the imposition of a short-term exposure limit does not necessarily require any reduction in cumulative exposure below the PEL, but instead addresses only short-term exposures *within* the PEL. It is therefore necessary to know, before imposing a short-term exposure limit, whether the short-term exposures sought to be regulated pose any risks to human health other than the contribution that they make to cumulative exposure (which is already controlled by the PEL).[7] It is thus critical to have evidence regarding the potential dose-rate effect of a substance[8] before a decision can be made to impose a short-term exposure limit.[9]

---

[7] PCHRG suggests that where the PEL still permits significant risk, a short-term exposure limit should be required to further reduce cumulative exposure. As an initial matter, the EOIC strongly disagrees that a PEL of 1 ppm permits any significant risk. Even assuming *arguendo,* however, that there is some significant risk remaining at the 1 ppm level, a short-term exposure limit would have to bring cumulative exposure below 1 ppm in order to make

B. Data On Dose-Rate Effects Are Of Particular Importance For EO, Because The PEL Will Itself Result In Low Short-Term Exposure Levels

Data on dose-rate effects are especially necessary in the case of EO, because the record amply demonstrates, as OSHA specifically found, that compliance with the PEL will, in and of itself, require control of short-term exposure levels.

The 1 ppm PEL, as a mathematical matter, sets an effective short-term exposure limit of 32 ppm, measured over a fifteen-minute interval. This 32 ppm limit can be reached only if exposure is zero for the rest of the day. Because background exposure is likely to occur in all facilities, including sterilization facilities, the practical short-term exposure limit set by a PEL of 1 ppm is actually considerably lower than the theoretical 32 ppm level. Moreover, due to the possibility of process variations, the controls used to meet the 1 ppm PEL must actually be designed to achieve a level considerably below 1 ppm (TWA). This level of control as a practical matter also reduces the theoretical 32 ppm level.

---

any real contribution to the reduction of such risk. However, OSHA has specifically found, and PCHRG has accepted the finding, that it is infeasible to reduce cumulative exposure below 1 ppm.

[8] This "evidence" need not always be experimental data specifically demonstrating a dose-rate effect. Under appropriate circumstances, information on pharmacokinetic, metabolic and mechanistic factors may be sufficient to allow extrapolation from chronic data in order to determine the likelihood of a dose-rate effect.

[9] PCHRG notes (PCHRG brief at 42-43) that OSHA has in two other cases imposed short-term exposure levels without citing data on dose-rate effects. The validity of those standards is not before this Court. We would note, however, that both of those standards were issued before the Supreme Court's decision in *Industrial Union Department, AFL-CIO* v. *American Petroleum Institute, supra.*

In addition, employers are strongly encouraged by the standard to use all feasible means to achieve exposure levels below the action level of 0.5 ppm (TWA). To achieve the action level, employers will have to reduce short-term exposures to less than half of the theoretical maximum allowed by the 1 ppm PEL.

Perhaps more importantly, the types of controls that will need to be employed to meet the PEL will also result in low short-term exposures. As the EOIC explained in its submissions to OSHA, employers seeking to reduce overall exposures will necessarily focus on and control short-term levels as well. This position is completely supported by the record.

For example, Dr. Roy, an OSHA witness at the hearing, stated in his written testimony that:

> The required control technology for a 15 ppm short-term limit is part of the control technology necessary to achieve the 1 ppm PEL, that is, in an operation where peak exposures are the primary basis for the overall employee exposure, the peaks must be controlled so that the time weighted average can be reduced.

(Exhibit 21-8). At the hearing, Dr. Roy reiterated that it would be necessary to control short-term exposures in order to comply with a PEL of 1 ppm. (Tr. 216, 263).[10]

---

[10] Dr. Roy's position was supported at the hearing by Mr. Howard Kuznetz (Tr. 823-24, 826-27), Ms. Carolyn Phillips (Tr. 960-63) and Dr. Larry Rampy (Tr. 967). As these witnesses explained, a company wishing to reduce exposure would develop a process profile of potential exposures and would then work to reduce the high potential exposures. One way to do this would be to set internal operating guidelines for short-term exposures designed to assist in achieving the desired PEL. These internal guidelines would be set on a plant-by-plant basis, depending on the exposure profile. As PCHRG is well aware, these internal operating guidelines are the type of controls adopted by Shell and Texaco. There is thus no factual basis for the suggestion in PCHRG's brief (p. 21 n.10) that Texaco and Shell support a short-term exposure limit.

NIOSH, in its peer review comments, also indicated that compliance with the PEL will require control of short-term exposures. In this respect, NIOSH stated that the 1 ppm PEL will actually require employers to maintain workplace concentrations near 0.5 ppm (to ensure that random variation does not result in exposures above the PEL), and that "it appears that *some* short-term exposure limit is necessary in order to satisfy the employer that the 1 ppm PEL has not been exceeded." (Exhibit 181 (emphasis supplied)). Although NIOSH suggested that this engineering need supports the issuance of a short-term exposure limit, it in fact demonstrates just the opposite. Given that employers will, as an engineering matter, need to adopt internal limits for short-term exposures, there is no reason for OSHA, in the absence of data on dose-rate effects, to select a single, arbitrary limit that would apply to all workplaces.[11]

---

[11] Other reasons also indicate that the new PEL will result in effective control of short-term exposures. It is a fundamental tenet of good industrial hygiene to comply with a PEL that control of overall exposure levels includes control of excursion levels as well. In this regard, the American Conference of Governmental Industrial Hygienists suggests that, as an indication of good *process* control, exposures should not exceed three times the TWA for more than 30 minutes per work day and should not exceed five times the TWA. (*See* Exhibit 155). Although these guidelines are not easily applicable to very low TWA's or to processes involving episodic exposure fluctuations, they indicate that the trained industrial hygienists who will be involved in implementing controls to achieve the PEL will also act to reduce short-term exposures. Moreover, compliance with the PEL will, as OSHA acknowledged in the preamble to the standard, 49 *Fed. Reg.* at 25778-79, and as Dr. Dixon noted in his peer review comments (Exhibit 187), already require the use of respirators when employees might be exposed to higher, short-term levels of EO. Other provisions of the standard, such as requirements for employee education and training and the preparation of written compliance plans, will ensure that both employers and employees are aware of potential higher exposures. This in turn will lead to the institution of measures to assure control of such exposures.

Because the PEL will itself require each employer to achieve some, fairly low short-term exposure level as part of its compliance program for the PEL, it would be particularly inappropriate to require that a specific short-term exposure limit be maintained by all employers, without evidence that such a specific limit is needed to protect employee health. Absent data on dose-rate effects, such a determination simply can not be made.

C. The Record Amply Demonstrates The Need Fo Dose-Rate Data

Contrary to the unsupported PCHRG assertion that the issue of dose-rate effects did not arise until OSHA made the decision to seek further information on the issue of a short-term exposure limit, the record is replete from its very beginning with comments regarding the need for such data. For example, the EOIC comments in response to the ANPR (Exhibit 4-33) stated: (1) that a short-term exposure level could only be justified if it could be shown that such exposures posed a significant risk apart from their contribution to cumulative exposure; (2) that extrapolation from chronic effects would require metabolic and pharmacokinetic data that would allow a determination of the specific effects of short-term exposures;[12] and (3) that there was no way of knowing from the various studies whether there were effects from short-term, high level exposures that were independent of the results of cumulative exposures of which the short-term exposures were a part.

The discussion of dose-rate data continued at the OSHA hearing. Dr. Golberg explained that data from the available chronic studies could not be used to come to any conclusion as to the need for a short-term exposure limit, without information on matters such as pharmacokinetics that would provide evidence of effects specifically related to short-term exposures. (Tr. 494,[13] 553-54). Dr. Golberg emphasized that such studies should consider the biologically effective dose (the dose actually delivered to the target tissues) rather than just ambient air concentrations, and noted that techniques are available to permit measurement of target doses in various organs. (Tr. 553-54). Dr. Janice Yager, principal author of a study that has been cited in support of a short-term exposure limit, cautioned that data on dose-rate effects would be necessary before her study could be used to determine the propriety of such a limit. In this regard, she testified at the hearings:

---

[12] In this respect, the EOIC noted scientific evidence indicating that short-term higher exposures would present *less* risk than equivalent exposures over a longer period. (*Id.*)

> This worker study, Yager, 1983, is the sole published study to date in which the transiently high breathing zone exposures experienced by sterilizer operators were characterized and a biological endpoint measured. However, because of limited numbers of observations, this data alone does not provide sufficient information on which to base a definitive standard.
>
> Additional data obtained by conducting controlled animal inhalation experiments in which cumulative dose is held constant while dose rate is varied are needed in order to substantiate or refute the dose equivalence concept for the SCE response. Animal inhalation studies designed to address the issue have been proposed.[14]

(Tr. 130).

---

[13] The OSHA transcript has two consecutive pages marked 494. The above reference is to the first such page.

[14] Dr. Yager further elaborated on the issue in response to questioning:

> *MR. BARNARD*: As I understand it, you regard your study now as being a screening or a preliminary study or at least a study which is not definitive or final and you are proposing additional studies to determine what the differences are between a cumulative exposure and a long-term exposure?
>
> *DR. YAGER*: Yes. I think that the significance of the study lies in the fact that when one does do a careful job of docu-

The need for data on dose-rate effects was further addressed in the peer review comments. Each of the selected peer reviewers received copies of the relevant parts of the transcript, as well as copies of the relevant studies, exhibits and prepared testimony.

The Environmental Mutagen Society (Exhibit 186) asked a committee comprised of three of its prominent cellular biologists and geneticists to review the issue. Each of the committee members independently concluded "that at this time there has been no scientific evidence presented for ethylene oxide which in any way supports the imposition of a STEL of 10 ppm for any 15-minute period." In explaining its conclusion, the committee stated:

> The prime issue as we all see it (and have each done considerable research on in our careers) is one of dose and dose-rate. Namely, is the biological outcome (the yield of induced damage) affected by the manner and delivery of the dose (exposure)? The evidence required to support a STEL would have had to demonstrate that for some endpoint . . . there was a *greater yield* of damage (effect) from an acute treatment as compared to a chronic or fractional treatment for *the same total dose*. No such evidence was presented.

(Exhibit 186) (emphasis in original). The committee further noted that dose-rate effects may occur only in one portion of the dose-response curve (normally at higher doses), and that there may very well not be such an effect at the low exposures permitted by the 1 ppm PEL.

> menting these high exposures that everyone talks about, but rarely measure, then it seems like there may be an effect on SCEs, but it is not clear whether that occurs from exclusively a cumulative component or exclusively a dose rate or in fact, unfortunately, a much more complicated situation where it may be both factors contributing.

(Tr. 124-35).

Similarly, the American Academy of Industrial Hygiene ("AAIH") concluded that a showing of dose-rate effects is necessary before a short-term exposure level could be justified. (Exhibit 175). The AAIH specifically noted that various studies relied on by supporters of a short-term exposure limit do not provide sufficient information to determine the importance, if any, of dose-rate, and that one study, that by Pero *et al.* (Exhibit 6-13), suggests that constant exposure may be of greater concern than equivalent intermittent exposures. AAIH recommended further research, and concluded, based on a review of the record materials, that "a short-term exposure level is not supported by appropriate scientific findings which suggest the elimination or reduction of a significant risk of harm."

The American Occupational Medical Association (Exhibit 187) asked "two highly-respected physician members" to prepare comments. Dr. Ernest Dixon stated that: (1) any significant risks posed by EO appear to be related to chronic exposure; (2) none of the studies relied on to support a short-term exposure limit effectively addresses short-term exposures; (3) that long-term studies can not be used to address potential short-term effects; (4) that the 1 ppm PEL and 0.5 ppm action level provide adequate protection from short-term effects; and (5) that a short-term exposure limit would result in only a miniscule, if any, reduction of overall exposure. Dr. Arnstadt concluded that no direct evidence exists to support a short-term exposure limit, or to calculate a particular value for such a limit, and that there are no data regarding the necessary issue of dose-rate effects. He further opined that the 1 ppm PEL is a "good, safe number with a safety margin for a possible dose-rate effect."

Thus, despite PCHRG's attempt to ignore the issue of dose-rate effects, it is clear that this question is central to the propriety of PCHRG's request that OSHA be ordered to impose a short-term exposure limit.

II. THERE ARE NO SCIENTIFIC DATA TO SUPPORT A SHORT-TERM EXPOSURE LIMIT

A. The Available Studies Do Not Support A Short-Term Exposure Limit

As determined by OSHA, the available studies do not contain sufficient data to support a short-term exposure limit. In particular, the studies relied upon by PCHRG—Hemminki *et al.* (Exhibit 6-7), Yager *et al.* (Exhibit 6-15) and Johnson & Johnson (Exhibit 137)—are inadequate to support the issuance of a short-term exposure limit. These studies were all provided by OSHA to the peer reviewers whose comments are cited above.

The methodological shortcomings of the Hemminki study, which the EOIC believes prevent any conclusion that EO was responsible for the reported reproductive effects, have previously been discussed at length. (*E.g.*, Exhibits 11-57, 62 through 67, 141 items C and E, 153). The EOIC will not repeat those comments here, but would instead merely point out that OSHA itself was only able to conclude in the preamble to the final standard that the study "suggests" that women exposed to EO "may be" at an increased risk. 49 *Fed. Reg.* at 25749. Certainly the Supreme Court decision in *Industrial Union Department, AFL-CIO v. American Petroleum Institute*, requires more than a mere suggestion of a possible association with harm before OSHA can find that there is substantial evidence of a significant risk.

The consideration that is by itself sufficient to eliminate the Hemminki *et al.* study from use in determining the need for a short-term exposure limit is that, despite PCHRG's repeated assertions of exposures below 1 ppm (TWA), *there were no exposure measurements taken in connection with the study.* The published report of the Hemminki study did provide some information regarding allegedly typical exposure levels in Finnish hospitals. However, that information was based on measurements that were not made in connection with the study.[15] Instead, the reported measurements were taken by the Department of Industrial Hygiene and Toxicology ("IHT") of the Finnish Institute of Occupational Health, pursuant to a consultation agreement with industry under which the IHT takes exposure measurements only upon request. Not only were the IHT measurements not necessarily representative of the hospitals that participated in the Hemminki *et al.* study, they did not even relate to the same time period as the study. The Hemminki *et al.* study covered the years 1950-1980, whereas IHT measurements only began in 1976 (two measurements) and were mostly taken in 1979 or later.[16]

At the hearing, Dr. Hemminki explicitly cautioned that the exposure data presented in his report should not be considered as related to the observed effects. Dr. Hemminki acknowledged that no industrial hygiene data were taken during the study and stated that "[w]e just thought of giving [the reported information] as information on general levels of ethylene oxide, but by no means would we have tried to correlate the spontaneous abortions to known levels of ethylene oxide." (Tr. 775).

---

[15] Information regarding the industrial hygiene data presented in the Hemminki report can be found in the EOIC report of its meeting with Dr. Hemminki, which was reviewed and signed by Dr. Hemminki (Exhibit 64).

[16] Furthermore, the measurements were primarily brief (less than one second) grab samples, which cannot be considered an adequate representation of human exposure in a dynamic work environment. In a few cases, these grab samples were supplemented by a single short-term (less than 20 minutes) bag sample. These bag sample readings ranged from 1 to 17 ppm. It is impossible to use these measurements to calculate an eight-hour time-weighted average. Because exposures were only measured for short-term periods, and because the lowest limit for the detection and sampling methods used is about 1 ppm, significant background exposures could have been missed. Both the IHT and Dr. Hemminki have agreed that it was improper to calculate eight-hour TWAs from these short-term samples. (Exhibit 64, Tr. 649-650).

The studies by Yager *et al.* and Johnson & Johnson are similarly deficient with respect to the issue of dose rate. The Yager *et al.* study found increased levels of certain cytogenetic changes, known as sister chromatid exchanges ("SCEs"), among a small number of hospital employees exposed to EO.[17] The only industrial hygiene measurements taken in connection with the study were short-term measurements of job tasks where exposure was known to occur.[18] Dr. Yager herself emphasized that these data can not be used to determine the need for a short-term exposure limit, because they do not demonstrate whether the effects are related to dose rate. She noted that research has been proposed to fill this need. (See p. 13 *supra*).

Dr. Julian Preston, Senior Research Staff Member, Oak Ridge National Laboratory, also addressed the limitations of the Yager study:

> The data of Yager *et al.* have frequently been quoted as indicating that short-term exposures are more effective at inducing SCE than the same dose given over say an eight-hour work day, *i.e.*, the frequency of SCE is influenced by dose rate. It is important to

---

[17] As discussed at pp. 20-22 below, SCEs and chromosome aberrations in peripheral lymphocytes are not predictive of adverse human health effects. Indeed, OSHA itself concluded in the preamble to the standard that "cytogenetic data can not be used to quantify the excess risk of disease caused by EtO exposure" and that cytogenetic tests can not be used to predict risk to an individual. 49 *Fed. Reg.* at 25747, 25788.

[18] It is totally inappropriate to take these measurements, as PCHRG has done, and attempt to convert them into an eight-hour time-weighted average. (*E.g.*, PCHRG brief at 11 n.5). There were no eight-hour measurements taken during the study. The lowest limit of detection for the instrument used to make the measurements (a Miran 1A) is about 1 ppm. When exposure levels for a job task got below the detection level, Dr. Yager and her colleagues ceased measuring. There is thus no basis for assuming, as the PCHRG calculation admittedly does, that there was no exposure other than during the specified tasks. Moreover, a Miran 1A is an area monitor, and can at best give only an approximation of actual employee exposure. (Tr. 1338 (Dr. Malcolm Ridgway)).

> note (a) that the high exposure group is very small, (b) there is no difference in SCE frequency between the low exposure group and the control *i.e.*, a dose response curve cannot be determined for the data set. In order for the conclusion to be drawn that short-term exposures to EtO are more effective at inducing SCE in human peripheral lymphocytes than the same dose received over a long time period, such as an eight-hour working day, data for both exposure conditions have to be available and obtained by the same laboratory preferably coincidentally. This is not the case for the study by Yager *et al.*, where no results for extended low-level exposures are available. . . . The increase in SCE seen in the high exposure group is probably caused by EtO, at a particular *accumulated* dose of [greater than] 100 mg, but cannot be assumed to be specifically due to the fact that this dose was received in intermittent high dose exposures. It is quite feasible to predict that chronic exposures would be more effective than intermittent high dose-rate exposures, as a result of, for example, saturation of DNA repair capacity.

(Exhibit 189-16 Appendix A) (citations omitted) (emphasis in original).

Dr. Golberg similarly stated that he agreed with Dr. Yager that it is scientifically inappropriate to use her data for the purpose of determining the need for a short-term exposure limit. (Exhibit 141 Item A). The peer review committee of scientists from the Environmental Mutagen Society also concluded that the Yager study could not be used to determine dose-rate effects or to serve as scientific evidence to support a short-term exposure limit. (Exhibit 186).

The Johnson & Johnson study has similar limitations. As Dr. Preston stated:

> The data reported by Johnson & Johnson to date on the induction of SCE in persons occupationally exposed to EtO do indicate that there are some in-

> creases in some of the exposed groups at some of the sampling times when compared to worksite controls. However, the interpretation and significance of the data is somewhat handicapped by the very small number of individuals in some of the exposed groups, and also by the potential influencing factor of inter-scorer variation. In addition, it is not possible from the data as presented to relate individual exposure or type of exposure to SCE or chromosome aberration frequencies. For these reasons it is not possible, even if it were desired, to relate frequencies of SCE to the same exposure received chronically as long-term, low exposure rate exposures or intermittently as short-term, higher exposure rate exposures. In addition, as has been discussed already, since SCE frequencies will at best only be indirectly related to exposure, whether chronic or acute, it is not possible to determine the need for or an appropriate value for a STEL from such data.

(Exhibit 189-16 Appendix A). These limitations on the Johnson & Johnson study were also noted by the Environmental Mutagen Society (Exhibit 186) and the American Occupational Medical Association (Exhibit 187).

In addition to these methodological limitations, the record supports the further conclusion that the Yager and Johnson & Johnson studies cannot properly be used in determining the need for a short-term exposure limit because the endpoint that they measured, SCEs and chromosome aberrations in peripheral lymphocytes, are not known to be predictive of adverse human health effects.

Perhaps the most complete discussion in the record of the lack of information on any relationships between cytogenetic changes induced in peripheral lymphocytes by chemicals and adverse health effects was that provided by Dr. Preston (Exhibit 189-16 Appendix A). In his comments on the matter, he explains that the mechanism for induction of chromosomal aberrations and SCEs in peripheral lymphocytes differs substantially for chemical agents as opposed to radiation.[19] He further stated that: (1) there is no indication that an increase in SCE is directly responsible for any other cellular change; (2) increases in SCE are not representative of chromosomal changes that may be indicative of adverse health effects; (3) chromosomal aberrations have been linked to adverse health effects only when they occur in germ cells, or perhaps non-differentiated somatic cells, *not* peripheral lymphocytes; and (4) it is currently impossible to extrapolate from chemically-induced aberrations in peripheral lymphocytes to aberrations in germ cells, much less to potential health effects. In conclusion, Dr. Preston stated:

> Thus, measurement of SCE in peripheral lymphocytes is not now known to be a predictor of subsequent adverse health effects, and data obtained cannot be used for setting exposure standards. Similarly, measurements of chromosome aberrations in peripheral lymphocytes in cases of chemical exposure cannot currently be used to estimate adverse health effects, and so also cannot be used in performing risk assessments or for setting exposure standards.

Id. (citations omitted).

The lack of a known relationship between cytogenetic changes in peripheral lymphocytes and adverse health effects, and the impossibility of using such changes to determine the need for exposure standards, was also noted by, among others, Dr. Golberg (Exhibit 47, Tr. 487), Dr. Joseph Grisham (Exhibit 49), the American Occupational Medical Association (Exhibit 187), the American Academy of Industrial Hygiene (Exhibit 175), and Dr. Vernon L. Carter (Exhibit 178). NIOSH, which supported a short-term exposure limit, and OSHA witness Dr. Marvin Legator also agreed that chemically-induced cytogenetic changes are not predictive of adverse human health effects. (Exhibit 11-146, Tr. 85). Accordingly, each recommended against the inclusion in the standard of medical tests for such effects. *Id.*

---

[19] Dr. Preston also explained that, contrary to PCHRG's attempt to dramatize SCEs by depicting switches of chromosome parts, such changes *do not in fact occur in peripheral lymphocytes in the body*. These cells are normally non-replicating cells and the effect is only manifested when they are removed from the body and induced to replicate *in vitro*. (Tr. 1001-1006, Exhibit 189-16 Appendix A).

B. PCHRG's Speculations On Dose-Rate Effect Do Not Provide Substantial Evidence

Despite the overwhelming record evidence demonstrating the absence of necessary data on dose rate, PCHRG has attempted to create the impression that such evidence is present in the record. Neither of the two speculations that PCHRG presents constitutes the type of substantial evidence necessary to support a short-term exposure limit.

First, PCHRG quotes from a portion of an internal OSHA memorandum discussing the Hemminki *et al.* study which states that a dose-rate effect is implicit in transplacental hazards because of the general existence of thresholds and the generally steep slopes of dose-response curves. (PCHRG brief at 43-44). Even apart from the fact that this statement is not based on any data regarding EO, it cannot support a short-term exposure limit. The existence of a threshold and a steep dose-response curve only indicates that there is a dose *response.* It does not provide any information about the role of dose *rate.*[20] As Dr. Generoso (Oak Ridge Laboratory) commented regarding the Hemminki study (involving possible transplacental effects—spontaneous abortions), as part of the Environmental Mutagen Society peer review, "[w]hat is clear . . . is the fact that this study has no bearing whatsoever on the question of dose-rate effect." (Exhibit 186).

The second piece of "evidence" put forward by PCHRG is a NIOSH statement that short-term higher exposures may exceed the cell's ability to repair itself. However, this statement is only one plausible explanation, and is therefore mere speculation. Dr. Preston observed that "[i]t is quite feasible to predict that chronic exposures would be more effective than intermittent high dose rate exposures, as a result of, for example, saturation of DNA repair capacity." (Exhibit 189-16 Appendix A). DNA repair capacity may well be less influenced by a specific dose at a particular time than by the existence of an interval between doses during which the repair mechanisms can operate.

---

[20] It is, of course, conceivable that a dose-rate effect could be responsible for such a dose-response curve. However, it is at least equally likely that this curve could be the result of a saturable mechanism or defense that is related to cumulative dose.

Thus the PCHRG speculations hardly constitute substantial evidence.

III. OSHA HAS MADE THE APPROPRIATE RESPONSE OF REQUESTING FURTHER STUDY

In face of the overwhelming record evidence demonstrating the need for, and absence of, data regarding dose-rate effects, OSHA has quite properly urged that further research be undertaken. The EOIC believes that any such research should consider the dose range of concern for actual human exposures, should utilize endpoints that have an established relevance to human health, and, as Dr. Golberg has emphasized, should look at target organ delivered dose as well as ambient air concentrations. It may also be possible, as the EOIC has noted, to develop data on pharmacokinetic and mechanistic factors that would allow extrapolation from chronic studies to short-term effects. Until evidence of this kind is developed, there simply is no scientific basis for promulgating a short-term exposure limit for EO.

CONCLUSION

For the foregoing reasons, the Ethylene Oxide Industry Council respectfully submits that this Court should uphold the OSHA decision not to promulgate a short-term exposure limit for ethylene oxide.

Respectfully submitted,

ROBERT C. BARNARD
ERIC C. JEFFREY
CLEARY, GOTTLIEB, STEEN
& HAMILTON
1752 N Street, N.W.
Washington, D.C. 20036
(202) 728-2700
Counsel for Amicus Curiae
Ethylene Oxide
Industry Council

Of Counsel:
DAVID ZOLL
General Counsel
CHEMICAL MANUFACTURERS
ASSOCIATION
2501 M Street, N.W.
Washington, D.C. 20037
(202) 887-1100

May 8, 1985